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Liver and Kidney Transplantation: A Half-Century Historical Perspective 435
David A. Sass and Alden M. Doyle

This article describes the evolution of solid organ kidney and liver transplantation and expounds on the challenges and successes that the early transplant researchers and clinicians encountered. The article highlights the surgical pioneers, delves into the milestones of enhanced immunosuppression protocols, discusses key federal legislative and policy changes, and expounds on the ongoing disparities of organ supply and demand and the need for extended criteria and live donor organs to combat these shortages. Finally, recent changes in organ allocation and distribution policies are discussed. The authors also spotlight novel interventions that will further revolutionize abdominal transplantation in the next 50 years.

From Child-Pugh to Model for End-Stage Liver Disease: Deciding Who Needs a Liver Transplant 449
Sheela S. Reddy and Jesse M. Civan

This article reviews the historical evolution of the liver transplant organ allocation policy and the indications/contraindications for liver transplant, and provides an overview of the liver transplant evaluation process. The article is intended to help internists determine whether and when referral to a liver transplant center is indicated, and to help internists to counsel patients whose initial evaluation at a transplant center is pending.

Renal Transplantation in Advanced Chronic Kidney Disease Patients 465
Mythili Ghanta and Belinda Jim

Kidney transplantation is the best option for patients with end-stage kidney disease. It is associated with better quality of life, lower medical costs, less hospitalization, and improved survival compared with wait-listed patients who remain on dialysis. Timely referral for transplantation is essential to reap the maximal benefit and should begin in the advanced chronic kidney disease stage prior to starting dialysis. Shortage of donor organs remains the biggest challenge to transplantation. With the improved success of kidney transplantation, candidate acceptance criteria continue to broaden. This article provides an overview of the pretransplantation multidisciplinary evaluation process detailing the factors that determine transplant candidacy.
Management of the Liver Transplant Recipient: Approach to Allograft Dysfunction
Jonathan M. Fenkel and Dina L. Halegoua-DeMarzio

Liver transplant (LT) recipients are living longer than ever today and many will experience some form of allograft dysfunction. The common causes of allograft dysfunction vary significantly depending on the timing since LT. Most allograft abnormalities are manageable with minimally invasive procedures, medications, and lifestyle modification. The most common differential diagnoses by time period after LT, and diagnostic and management considerations, are highlighted. Collaboration and comanagement of LT recipients between primary care and the transplant hepatologist is essential for optimizing recipient and allograft outcomes.

Acute and Chronic Allograft Dysfunction in Kidney Transplant Recipients
Ryan J. Goldberg, Francis L. Weng, and Praveen Kandula

Allograft dysfunction after a kidney transplant is often clinically asymptomatic and is usually detected as an increase in serum creatinine level with corresponding decrease in glomerular filtration rate. The diagnostic evaluation may include blood tests, urinalysis, transplant ultrasonography, radionuclide imaging, and allograft biopsy. Whether it occurs early or later after transplant, allograft dysfunction requires prompt evaluation to determine its cause and subsequent management. Acute rejection, medication toxicity from calcineurin inhibitors, and BK virus nephropathy can occur early or later. Other later causes include transplant glomerulopathy, recurrent glomerulonephritis, and renal artery stenosis.

The ABCs of Immunosuppression: A Primer for Primary Care Physicians
Gregory Malat and Christine Culkin

Immunosuppression use for prevention of allograft recognition/rejection has evolved to reflect an expanded understanding of the immune system, as well as a fine tuning of the goals of therapy. Immunosuppression in organ transplantation represents a balance between the desire to improve the health status of an individual affected by chronic conditions versus not imposing an unintended immunodeficiency leading to iatrogenic morbidity/mortality. This article discusses the selection and general dosing of immunosuppression in organ allograft recipients to allow providers to be comfortable in monitoring immunosuppressive therapy long term and the associated, expected posttransplant complications in allograft recipients.

Managing Cardiovascular Risk in the Post Solid Organ Transplant Recipient
Mrudula R. Munagala and Anita Phancao

Solid organ transplantation is an effective treatment for patients with end-stage organ disease. The prevalence of cardiovascular diseases (CVD) has increased in recipients. CVD remains a leading cause of mortality among recipients with functioning grafts. The pathophysiology of CVD recipients is a complex interplay between preexisting risk factors, metabolic sequelae of immunosuppressive agents, infection, and rejection. Risk modification must be weighed against the risk of mortality owing to rejection or infection. Aggressive risk stratification and modification before and after transplantation and tailoring immunosuppressive regimens are
essential to prevent complications and improve short-term and long-term mortality and graft survival.

**Diabetes Care After Transplant: Definitions, Risk Factors, and Clinical Management**  
Amisha Wallia, Vidhya Illuri, and Mark E. Molitch

Patients who undergo solid organ transplantation may have preexisting diabetes mellitus (DM), develop new-onset DM after transplantation (NO-DAT), or have postoperative hyperglycemia that resolves shortly after surgery. Although insulin is usually used to control hyperglycemia in the hospital, following discharge most of the usual diabetes oral and parenteral medications can be used in treatment. However, when there are co-morbidities such as impaired kidney or hepatic function, or heart disease, special precautions may be necessary. In addition, drug-drug interactions, such as drugs interacting with CYP3A4 enzyme pathway, require additional consideration because of possible interaction with immunosuppressive drug metabolism.

**De Novo Malignancies After Transplantation: Risk and Surveillance Strategies**  
Iliana Doycheva, Syed Amer, and Kymberly D. Watt

De novo malignancies are one of the leading causes of late mortality after liver and kidney transplantation. Nonmelanoma skin cancer is the most common malignancy, followed by posttransplant lymphoproliferative disorder and solid organ tumors. Immunosuppression is a key factor for cancer development, although many other transplant-related and traditional risk factors also play a role. In this review, the authors summarize risk factors and outcomes of frequently encountered de novo malignancies after liver and kidney transplantation to stratify recipients at highest risk. Future efforts in prospectively validated, cost-effective surveillance strategies that improve survival of these complex patients are greatly needed.

**Metabolic Bone Disease in the Post-transplant Population: Preventative and Therapeutic Measures**  
Johan Daniël Nel and Sol Epstein

Post-transplant bone disease contributes significantly to patients’ morbidity and mortality after transplantation and has an impact on their quality of life. This article discusses the major contributors to mechanisms causing bone loss, highlighting the role of preexisting disease in both kidney and liver failure and contributions from glucocorticoids and calcineurin inhibitors. Suggested monitoring and investigations are reviewed as well as treatment as far as the current literature supports, emphasizing the difference between kidney and liver recipients.

**Infectious Complications and Vaccinations in the Posttransplant Population**  
William G. Greendyke and Marcus R. Pereira

Infections remain a major cause of mortality and morbidity after both kidney and liver transplantation, and internists increasingly play a major role in diagnosing and treating these infections. Because of immunosuppression, solid organ transplant recipients do not often demonstrate classic signs
and symptoms of infection and have a broader variety of common and opportunistic infections, many of which are generally more difficult to diagnose and treat. Although these patients have many risk factors for infection, a major determinant is the time after transplant as it relates to levels of immunosuppression, healing, and hospital or environmental exposures.

Selection and Postoperative Care of the Living Donor

Dianne LaPointe Rudow and Karen M. Warburton

Live organ donors typically consult their primary care providers when considering live donation and then return for follow-up after surgery and for ongoing primary care. Live liver and kidney transplants are performed routinely as a method to shorten the waiting time for a recipient, provide a healthy organ for transplant, and increase recipient survival. Careful medical and psychosocial evaluation of the potential donor is imperative to minimize harm. This evaluation must be performed by an experienced live donor medical team. Routine health care with careful attention to weight maintenance, cardiovascular health, and prevention of diabetes and hypertension is paramount.

Long-Term Functional Recovery, Quality of Life, and Pregnancy After Solid Organ Transplantation

Swati Rao, Mythili Ghanta, Michael J. Moritz, and Serban Constantinescu

This article reviews the salient features of functional recovery, health-related quality of life (HR-QOL), and reproductive health, with special emphasis on pregnancy outcomes in kidney and liver recipients. Transplantation results in improved functional status and HR-QOL. Addressing factors that limit the optimal rehabilitation of transplant recipients can improve transplant outcomes. After successful transplantation, there is a rapid return of fertility, warranting counseling regarding contraception. Practitioners should be aware of the teratogenic potential of mycophenolic acid products. Posttransplant pregnancies are high risk, with increased incidences of hypertension, preeclampsia, and prematurity. Most pregnancies in kidney and liver recipients have successful maternal and newborn outcomes.

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